### **PCT**

#### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: WO 99/65469 (11) International Publication Number: A3 A61K 9/16, 9/51, 9/14 (43) International Publication Date: 23 December 1999 (23.12.99)

PCT/US99/13755 (21) International Application Number:

(22) International Filing Date:

18 June 1999 (18.06.99)

(30) Priority Data:

60/089,852

19 June 1998 (19.06.98)

US

(71) Applicant: RTP PHARMA INC. [CA/US]; 4364 South Alston Avenue, Durham, NC 27713-2280 (US).

(72) Inventors: PACE, Gary, W.; 6913 Hunters Way, Raleigh, NC 27615 (US). VACHON, G., Michael; 445, rue Strathcona, Westmount, Quebec H3Y 2X2 (CA). MISHRA, K., Awadhesh; Appartement 201, 670 de Gaspe, Iles des Soeurs, Verdun, Quebec H3E 1H8 (CA). HENRIKSEN, Inge, B.; Lagaardsvegen 131, N-4010 Stavanger (NO). KRUKONIS, Val; 287 Emersion Road, Lexington, MA 02173 (US). GODINAS, Anthony; 30 Washington Street, Methuen, MA 01844 (US).

(74) Agent: CRAWFORD, Arthur, R.; Nixon & Vanderhye P.C., 8th floor, 1100 North Glebe Road, Arlington, VA 22201-4714 (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 2 March 2000 (02.03.00)

(54) Title: PROCESSES TO GENERATE SUBMICRON PARTICLES OF WATER-INSOLUBLE COMPOUNDS

#### (57) Abstract

Submicron particles of water-insoluble compounds, particularly drugs, are prepared by simultaneously stabilizing microparticulate suspensions of same with surface modifier molecules by rapid expansion into an aqueous medium from a compressed solution of the compound and surface modifiers in a liquefied gas and optionally homogenizing the aqueous suspension thus formed with a high pressure

## FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of Americ
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
СН	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
cz	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

## INTERNATIONAL SEARCH REPORT

Inte onal Application No PCT/US 99/13755

A. CLASSIF IPC 6	FICATION OF SUBJECT MATTER A61K9/16 A61K9/51 A61K9/14			
According to	o International Patent Classification (IPC) or to both national classification	tion and IPC		
	SEARCHED			
Minimum do IPC 6	cumentation searched (classification system followed by classificatio $A61K$	n symbols)		
	ion searched other than minimum documentation to the extent that su			
Electronic d	ata base consulted during the international search (name of data bas	e and, where practical, search terms used)		
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the rele	evant passages	Relevant to claim No.	
E	WO 99 52504 A (HOFFMANN LA ROCHE) 21 October 1999 (1999-10-21) the whole document		1-16	
A	WO 97 14407 A (RES TRIANGLE PHARMACEUTICALS ;UNIV TEXAS (US); HENRIKSEN INGE B (U) 24 April 1997 (1997-04-24) cited in the application the whole document		1-16	
А	WO 95 21688 A (WEIDNER ECKHARD ;K ZEŁJKO (SI); NOVAK ZORAN (SI)) 17 August 1995 (1995-08-17)	NEZ		
A	US 3 998 753 A (ANTOSHKIW THOMAS ET AL) 21 December 1976 (1976-12-			
	-	-/		
X Furt	her documents are listed in the continuation of box C.	X Patent family members are listed	in annex.	
"A" docume consic "E" earlier filing c "L" docume which citatio "O" docum other "P" docume later t	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another or or other special reason (as specified) entering to an oral disclosure, use, exhibition or means ent published prior to the international filing date but han the priority date claimed	T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family		
	actual completion of the international search  23 December 1999	Date of mailing of the international sea 12/01/2000		
	mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Authorized officer Fischer, W		

## INTERNATIONAL SEARCH REPORT

Int: .ional Application No PCT/US 99/13755

		PCT/US 99/13755		
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.	
<b>A</b>	G. DONSI ET AL.: "POSSIBILITY OF APPLICATION TO PHARMACEUTICAL FIELD" PHARM. ACTA HELV,1991 - 1991, pages 170-173, XP002900588			
	·			
	·			
	·			
:				

# INTERNATIONAL SEARCH REPORT

.nformation on patent family members

inte ional Application No PCT/US 99/13755

Patent document cited in search report		Publication date	Patent family member(s)		Publication date	
WO	9952504	Α	21-10-1999	NONE		
WO	9714407	A	24-04-1997	AU	709262 B	26-08-1999
				AU	7461796 A	07-05-1997
			•	EP	0855906 A	05-08-1998
WO	9521688	Α	17-08-1995	SI	9400079 A	31-10-1995
				AT	159184 T	15-11-1997
				CA	2182786 A	17-08-1995
				DE	59500808 D	20-11-1997
			•	DK	744992 T	02-06-1998
				EP	0744992 A	04-12-1996
				ES	2109095 T	01-01-1998
				GR	3025495 T	27-02-1998
				JP	9508851 T	09-09-1997
US	3998753	Α	21-12-1976	AT	351912 B	27-08-1979
			T.	· AT	625675 A	15-01-1979
				BE	832331 A	12 <b>-</b> 02-1976
				DE	2534091 A	26-02-1976
		•		FR	2281961 A	12-03-1976
				GB	1502895 A	08-03-1978
				IT	1050722 B	20-03-1981
				JP	51041732 A	08-04-1976
				NL	7509586 A	17-02-1976